

COMMENTS ON BEHALF OF

**Allergy and Asthma Network • Mothers of Asthmatics
American Academy of Allergy, Asthma and Immunology
American Association of Respiratory Care
American College of Allergy, Asthma and Immunology
American College of Chest Physicians
American Lung Association
American Thoracic Society
Asthma and Allergy Foundation of America
Joint Council on Allergy, Asthma, and Immunology**

**RE: FDA Proposed Rule
Use of Ozone Depleting Substances; Essential Use Determinations
Docket No. 97N-0023**

November 30, 1999

97N-0023

C9612

The organizations providing this comment represent the leading American patient advocacy and medical speciality groups concerned with respiratory diseases, particularly asthma. The Stakeholders Group on Metered Dose Inhalers was established in 1996 to assure these organizations' appropriate opportunities for participation as the United States addresses its obligations under the Montreal Protocol on Substances that Deplete the Ozone Layer, and the Clean Air Act Amendments of 1990. These obligations, in part, require the reformulation of metered dose inhalers that use chlorofluorocarbons as the propellant. The Stakeholders Group supports and encourages the development of a responsible strategy to provide for a transition to CFC-free metered dose inhalers. The stakeholders have previously commented on criteria for any transition strategy and these are appended to this statement.

While many of the Stakeholders concerns with the previous FDA Advance Notice of Proposed Rulemaking have been addressed in the Proposed Rule, there remain many important issues to be resolved as noted later in this comment. Given this, the Stakeholders continue to believe that the transition to CFC-free metered dose inhalers provides a unique opportunity for each member organization to refocus attention on the proper diagnosis and management of asthma and to revitalize the relationship between physicians and other health care providers and patients with asthma.

The Stakeholders have commented previously regarding the role of patient and professional education in any transition strategy. As noted in the European Union, education needs to reach a critical level when many new products are introduced in

rapid succession. The Stakeholders recognize that such education efforts do not fall within the jurisdiction of the Food and Drug Administration. However, the Stakeholders encourage the FDA to explore interagency mechanisms to insure coordination and collaboration with federal government entities having authority for educational efforts including the National Asthma Education and Prevention Program. Coordination and collaboration among federal government agencies, nongovernmental organizations representing patients and health care providers, including the pharmaceutical industry and managed care companies must occur to ensure a consistent and appropriate level of effort as reformulated products enter the marketplace. The Stakeholders look to the Agency for leadership in this critical area.

Comments Specific to the Proposed Rule

- **Moiety-by-Moiety Approach**

The Stakeholders concur with the “moiety-by-moiety” approach detailed in the Proposed Rule. This decision-making structure should continue to provide a range of treatment options for physicians and patients as the transition proceeds. It is critical that any decision-making scheme is structured to ensure that physicians remain able to treat patients effectively, following the national Asthma Education and Prevention Program Treatment Guidelines.

The Stakeholders also concur with the Proposed Rule requirement that more than one acceptable Non-Ozone Depleting Substance (ODS) alternative per action moiety be available prior to removing the essential use designation if there are multiple products or strengths of the moiety currently on the market. In this manner competition currently in place will remain to provide some economic checks and balances as new products are introduced.

- **Listing of Action Moieties**

Except as discussed below regarding additional approved products containing listed active moieties, the Stakeholders concur with the proposed reorganization of the list of essential uses to provide separately each currently marketed active moiety deemed essential. Such a listing will limit confusion as the transition proceeds.

- **Petitions to Add New Essential Uses**

The Stakeholders agree that it is inappropriate to add new essential uses that provide no new therapy at a time when developed nations including the United States have committed to the phase-out of the production and consumption of ozone depleting substances. The proposed approach with respect to new chemical entities significantly raises the evidentiary base for decision-making. In

particular, the Stakeholders support the criteria, “un-available important public health benefit,: including quantification of mortality and morbidity impacts.

While the Stakeholders appreciate the Agency’s provisions for determining the essentiality of new chemical entities, it remains unclear how the Agency will approach the issue of an application for a new product containing an active moiety already available in aerosol form. The continued approval of such ODS products is contrary to the spirit and intent of the Montreal protocol. The Agency’s view that overlapping jurisdictions leave it without statutory authority is unfortunate at a time when its leadership is critical to U.S. commitments under the Montreal Protocol. The Stakeholders believe that such authority is currently available within the mandates of both the Montreal Protocol and the Clean Air Act Amendments of 1990. This is particularly relevant when additional uses are considered for products that provide for no significant **therapeutic** innovation. In such instances, new approvals will serve only to make the FDA’s job of eliminating ozone depleting substances more difficult and costly.

- **Determinations of Continued Essentiality**

The Stakeholders concur with the decision-making process outlined in the Proposed Rule. In the first section, the Agency is to be commended for its common-sense approach of removing an active moiety from the essential use list if it is no longer marketed in an ODS formulation.

Under a second section, the Agency proposes a process, commencing after January 1, 2005, to review the essential use status of all current active moieties. FDA states that even if all current essential-use moieties are not reformulated, sufficient alternatives may exist to fully meet the needs of patients. Criteria proposed would ensure ODS products remain essential until a non-ODS product was marketed by the same route of administration, for the same indication, with the approximate level of convenience; that supplies and production capacity would be sufficient to meet patient need; that one year of post-marketing data was available; and that patients who medically require the ODS product are adequately served by available alternatives.

The Stakeholders believe it is critical to fully engage the patient and health care provider communities in this process. A notice and comment period plus consultations with an advisory committee are not sufficient to ensure input from a well-informed public. The Agency's experience with the Advance Notice for Proposed Rulemaking demonstrates the need for carefully prepared regulatory materials, patient, medical professional and public education, ample opportunity for interaction with Agency advisory bodies and personnel.

Additional Comments

- **Timeframe**

The Stakeholders are concerned that the proposed decision-making structures fail to provide a suggested timeframe for non-essential use determinations beyond the market review after January 1, 2005. We note only a timeframe of one-year for the collection of postmarketing studies. The Agency should provide patients, health care providers and the public with detailed timeframes including an estimation of time for any anticipated regulatory proceeding in addition to the content of information required. While there is no consensus at present on what constitutes an appropriate timeframe, the Agency should seek public comment on this important part of the transition.

- **New Non-ODS Product**

The Stakeholders remain concerned that FDA have sufficient resources to manage approval the anticipated number of applications for non-ODS metered dose inhalers in the coming years. While the Stakeholders would like to see a timely decision making process, patient health and safety remain a first concern as the transition proceeds.

- **Overall Monitorinn of Process**

The Stakeholders previously commented on the need to establish a mechanism to monitor the overall transition to non-ODS products. At a minimum, such a mechanism should include an expert panel appointed to assess baseline information from which to monitor all aspects of the transition. Panel members should include medical experts, other members of the health care team including nurse educators, pharmacists and respiratory therapists, epidemiologist and patients and patient advocates.

Criteria for a Transition Strategy

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Any transition strategy developed for the phase-out of CFC-containing MDIs should meet the following criteria:

- ensure product safety and efficacy,
- ensure patient acceptance through on-going patient education and monitoring and that the level of effort be consistent throughout the transition period,
- preserve the patient-physician relationship,
- provide a clearly defined timeframe for the transition to allow the health care provider to plan and implement treatment strategies and corresponding patient education activity,
- provide a mechanism to address product withdrawal, whether related to a CFC product for which there is a CFC-free alternative or a voluntary product withdrawal by a pharmaceutical company for which a CFC-free alternative does not exist,
- address cost concerns by providing that a CFC-free alternative is acceptable if its price is comparable to the product it replaces, on a daily therapy basis, and
- complete the phase-out of CFCs as an overall environmental and public health benefit in a timely and sensitive manner that balances patient issues and environmental goals without creating **unnecessary** delay or penalizing companies who have demonstrated action in advance of any Protocol decisions.

June, 1996

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From: Novella Abrams[nabrams@lungusa.org]
Sent: Tuesday, November 30, 1999 4:43 PM
To: Fdadoctors@oc.fda.gov
Subject: Filing of Written Comments



WordPerfect 6.1

The attached are written comments re: Docket No. 97N-0023, Use of
Ozone-Depleting Substances: Essential Use Determinations"

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